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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,541	10/28/2003	Stephen P.A. Fodor	56297-5003-21	3654

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COOLEY GODWARD LLP
THE BOWEN BUILDING
ATTN: THE PATENT GROUP
875 15TH STREET, N.W., SUITE 800
WASHINGTON, DC 20005-2221

EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/694,541	FODOR ET AL.	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-30 and 32-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-30 and 32-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed June 12, 2006. Currently, claims 26-30, 32-55 are pending. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.

2. Any objections and rejections not reiterated below are hereby withdrawn.

Maintained Rejections

Priority

1. This application claims priority to numerous applications dating back to December 6, 1990.

Drawings

2. The drawings are acceptable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 26-30, 34-36, 38-39, 42-51, 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drmanac et al. (EPO 392 546, October 17, 1990) in view of Ghosh et al. (Nucleic Acids Research, Vol. 15, No. 13, pages 5353-5372, 1987).

Drmanac et al. (herein referred to as Drmanac) teaches a process for determination of a complete or a partial contents of very short sequences in the samples of nucleic acids connected to the discrete particles of microscopic size by hybridization with oligonucleotide probes. Drmanac teaches the importance of detection of a large number of mapped polymorphic sites in genomic DNA of individual, family or population (col. 1-2). The polymorphic sequence detection through specificity which has hybridization with oligonucleotides (col. 2, lines 10-15). Drmanac teaches that the process is used for the determination and tracking of the heredity of the large number of the genomic or gene polymorphic sequences for identification of the person, determination of the relatedness or evolutionary distance, detection of the changes on

the genome and genes, prenatal and postnatal prediction of the phenotype characteristics, for example (col. 27, lines 45-50)(limitations of Claim 42, 44, 45). The Drmanac process presents improvements in preparation of samples for hybridization and improvements which enable one to follow gene expression by determining partial or complete fragment sequences of genomic DNA, mRNA or cDNA. Drmanac teaches by binding fragments of genomic DNA (ie. Nucleic acid molecules corresponding to RNA transcripts of one or more said genes, pool of DNA/RNA) to discrete particles (DP) of a microscopic size which are recognizable in a step of reading experimental image, the necessity for addressed samples on filters is dispensed with and this drastically reduces automatical-robotical component of the process and allows miniaturization of the entire method from a level of industrial installation to the level of laboratory instrument (limitations of Claim 35). The polynucleotide may be amplified from a sample, ie. amplification of genomic fragments (col. 6, lines 50-60; col. 12)(limitations of Claim 36, 51). Drmanac teaches solid particles carrying the required number of copies of the same DNA fragment attached to it surface. Aliquots of DPs from each well are mixed together and spread in the monolayer of required density and fixed. Hybridization areas are obtained similar to filters in dot blot procedures (col. 7, lines 25-30). Drmanac teaches three ways of recognizing DPs which can be combined. These include labeling with physical attributes of DP like size, shape and color which can be differentiated in a phase of reading such as during image analysis (col. 7, lines 45-50)(limitations of Claims 39). Moreover labeling with different combinations of ONs which can be recognized. This combination may be considered a unique species. Drmanac teaches

that by using 20 different oligonucleotides 300,000 different combinations can be formed with 10 oligonucleotides each (limitations of Claims 34-35). Drmanac teaches that the DP may be represented in the mixture once. DPs with the same oligonucleotide possess the same physical or chemical characteristics and discrete particles containing a different oligonucleotide can, by physical or chemical characteristics be identical or different by size, shape and color or can contain different oligonucleotide combination (col. 30, lines 15-17)(limitations of Claim 39, 54). Drmanac teaches the system must allow simultaneous discriminative hybridization on the level of one base pair mismatch (col. 21, lines 45-46)(limitations of Claim 43). By attaching each combination of oligonucleotides the particles 300,000 differentially labeled DPs are obtained (col. 7, lines 55-60). Drmanac teaches use of image analysis of microscopic monolayer hybridization layers (col. 10, lines 5-7). By forming a monolayer spread of DPs, detection by image analysis is permitted (col. 26, lines 10-13). Drmanac teaches synthesis of 100,000,000 particles each carrying a different longer ON (for examples, 16-mer)(limitations of Claim 27-29, 38, 48-50, 53). Drmanac teaches that the oligonucleotide probes have the length of 4-20 bases (col. 28, lines 46-48). Therefore, the discrete particles (i.e. beads, spheres or particles) comprises unique species of nucleic acids attached.

Drmanac does not specifically teach using nucleic acids between 25-100 nucleotides in length.

However, Ghosh teaches coupling of oligonucleotides 17-29 bases in length to solid supports derivitized with alkyl-amino and –carboxylic functionalities. Ghosh

specifically teaches that DNA immobilized on supports can be used for biochemistry and molecular biology for the detection, isolation and genetic analysis of specific DNA sequences. Ghosh teaches that their choice of oligonucleotides in the 20-50 base length range has been influenced by a number of factors including the use of automated nucleic acid synthesizers. Ghosh teaches the sequences allow sample to be screened quickly for the presence of target sequences.

Therefore, it would have been prima facie obvious at the time the invention was made to have modified the teachings of Drmanac which uses probes of 4-20 bases with the teachings of Ghosh for using probes of 17-29 bases. Ghosh specifically teaches the 20-50 base nucleotides allows for screening of presence of target sequences. Thus, the ordinary artisan would have been motivated to have made longer sequences in the range of 20-50 bases to detect target sequences. Ghosh specifically examines the chemistry and attachments of nucleic acids to the glass beads and obtains covalent attachment which allows further analysis on the solid beads.

5. Claims 26-28, 30, 34-38, 40-49, 51-53, 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern (WO 89/10977, November 16, 1989) in view of Ghosh et al. (Nucleic Acids Research, Vol. 15, No. 13, pages 5353-5372, 1987).

Southern teaches a new approach to produce fingerprint analysis (page 1). Southern teaches the use in the detection of single base changes in human genes including sickle cell disease (page 4)(limitations of Claim 30). Many alleles in a single analysis, by hybridization to an array of allelic pairs of oligonucleotides, greatly

simplifying the methods used to find linkage between a DNA polymorphism and phenotypic marker such as a disease gene (page 22, lines 30-35). Southern teaches the probe may comprise labeled sequences amplified from genomic DNA or a complete set of oligonucleotides (page 2)(limitations of Claim 36, 38, 51, 53). Other applications include analysis of known point mutations, genomic fingerprinting, linkage analysis, and sequence determination (abstract). Very stringent hybridization conditions that eliminate annealing to mismatch sequences or to oligonucleotides differing in length by as little as one base (page 19, lines 13-14). Southern teaches that the number of oligonucleotides analyzed could be quite large (page 22). Specifically fifty pairs made from selected alleles would be enough to give a fingerprint unique to an individual (page 22)(limitations of Claims 27, 28). Southern teaches that fluorescent probes are envisaged given the high concentration of the target oligonucleotides (page 14)(limitations of Claims 52, 55). The examples illustrate probe lengths of 19mers (page 18).

Southern does not specifically teach using beads for the point mutation analysis nor specifically teach using nucleic acids between 25-100 nucleotides in length.

However, Southern suggests oligonucleotide synthesis upon a solid support of controlled pore size glass (CPG). Southern teaches that the art did not previously directly use oligonucleotides as hybridization probes while still attached to the matrix to which they were synthesized.

Moreover, Ghosh teaches coupling of oligonucleotides 17-29 bases in length to solid supports derivitized with alkyl-amino and –carboxylic functionalities. Ghosh

specifically teaches that DNA immobilized on supports can be used for biochemistry and molecular biology for the detection, isolation and genetic analysis of specific DNA sequences. Ghosh teaches that their choice of oligonucleotides in the 20-50 base length range has been influenced by a number of factors including the use of automated nucleic acid synthesizers. Ghosh teaches the sequences allow sample to be screened quickly for the presence of target sequences.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have used oligonucleotides bound to beads for detection of point mutations. The ordinary artisan would have been motivated to have not removed the oligonucleotides from the beads and reattached on a solid support after synthesis, since Southern suggests that the beads themselves may be used as the support for hybridization. Southern further teaches that nucleic acids on supports may be used for point mutations analysis and detection of the nucleic acid on the support. The art teaches that CPG beads were used to synthesis oligonucleotides. Southern teaches that hybridization may be directly performed using the oligonucleotides as hybridization probes while still attached to the matrix beads. Thus, the ordinary artisan would have been motivated to have performed the point mutations analysis taught by Southern using the beads upon which the nucleic acid was synthesized to avoid the cleavage and reattachment steps which would have been previously required to remove and reattach the synthesized probes to a solid support.

Further, it would have been prima facie obvious at the time the invention was made to have modified the teachings of Southern which uses probes of 4-20 bases with

the teachings of Ghosh for using probes of 17-29 bases. Ghosh specifically teaches the 20-50 base nucleotides allows for screening of presence of target sequences. Thus, the ordinary artisan would have been motivated to have made longer sequences in the range of 20-50 bases to detect target sequences. Ghosh specifically examines the chemistry and attachments of nucleic acids to the glass beads and obtains covalent attachment which allows further analysis on the solid beads.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 26-35, 38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 22 of U.S. Patent No. 6,852,488

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by

or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentable distinct from each other because Claims 26-35, 38 of the instant application is generic to all that is recited in Claim 22 of U.S. Patent No. 6,852,488. That is, Claim 22 of 6,852,488 falls entirely within the scope of Claim 26-35, 38 or in other words, Claim 26-35, 38 is anticipated by Claim 22 of 6,852,488. Here, claim 22 of U.S. Patent No. 6,852,488 recites a method of detecting a mutation in a target nucleic acid sequence vs a known sequence by exposing a target sequence to at least one known core sequence where the core sequence is attached to a beach; determining the binding affinity to the target sequence and comparing affinity (i.e. hybridization) to detect a mutation. Claim 7 of '488 is drawn to probes of between 5-100 bases in length (instant Claims 31-33).

7. Claims 26-55 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-53of U.S. Patent No. 6,440,667.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d

1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentable distinct from each other because Claim 26-55 of the instant application is generic to all that is recited in Claim 1-53 of U.S. Patent No. 6,440,667. That is, Claim 1-53 of 6,440,667 falls entirely within the scope of Claim 26-55, or in other words, Claim 26-55 is anticipated by Claim 1-56 of 6,440,667. Here, claim 39, for example, of U.S. Patent No. 6,440,667 recites a method of identifying a target nucleic acid in a sample by contacting a target sample with a collection of beads that bear different probe nucleic acids and a probe encoding system. Based on hybridization, the different probes on the beads identify the target nucleic acid.

Response to Arguments

The response does not address the double patenting rejections.
Thus for the reasons above and those already of record, the rejection is maintained.

8. Claims 26-55 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-25 of U.S. Patent No. 6,544,739.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d

1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentable distinct from each other because Claim 26-55 of the instant application is generic to all that is recited in Claims 1-25 of U.S. Patent No. 6,544,739. That is, Claims 1-25 of 6,544,739 falls entirely within the scope of Claim 26-55, or in other words, Claim 26-55 is anticipated by Claims 1-25 1-56 of 6,544,739. Here, claim 23, for example, of U.S. Patent No. 6,544,739 recites a method of identifying different biological entities by providing a plurality of markers which comprise a different and unique nucleic acid, combining the sample with a unique and determinable nucleic acid sequence and identifying the sequence. Beads comprising a plurality of nucleic acid probes attached thereto are provided under hybridization conditions.

Response to Arguments

The response does not address the double patenting rejections.

Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

9. No claims allowable over the art.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Monahan et al. (EP 0 154 505) teaches diagnosis of gene abnormalities by

restriction maping using a sandwich hybridization format. The method of Monahan does not specifically teach a plurality of different target sequences. The method appears to teach analysis of a single polymorphism.

B) Malcolm et al. (WO 86/03782, July 1986) teaches sandwich hybridization for detection of nucleotide sequence.

C) Dattagupta et al. (EP 0 130 515 A2, January 9, 1985) teaches testing DNA samples for particular nucleotide sequences.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

J. Goldberg

Jeanine Goldberg
Primary Examiner
August 16, 2006